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Applications of Biomonitoring in Environmental Decision Making

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Outline

- Basic Concepts
- Potential Uses for Biomonitoring for Agency decisions
  - Approaches
  - Strengths
  - Current limitations
- How we move forward

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Concepts

- Biomarker – biochemical, molecular, genetic, immunologic or physiologic signal of events in biological systems
- Biomarkers of Exposure, Effect, Susceptibility
- ***Exposure Biomarker – The chemical or its metabolite or the product of an interaction between a chemical and some target molecule or cell that is measured in a compartment in an organism (NRC, 2006)***

Concepts

- Good Exposure Biomarker
  - Sensitive
  - Specific to the exposure of concern
  - Reproducible and reliable sampling methods
  - Reproducible and reliable analysis methods
  - Easy to collect, available, and inexpensive
  - Variability in the biomarker should be due to the variability in exposure
  - Biologically relevant (desired not necessary)

Concepts

- Biomonitoring must be used as one tool in an integrated system
  - Questionnaires-extant data
    - Sources and patterns of use
    - Human characteristics and activities
  - Environmental and personal measurement data
  - Biomarkers
  - Exposure models
  - PBPK models

Concepts

- Forward Dosimetry -biomarker concentrations are estimated using external exposure information with exposure and PBPK models

- Reverse Dosimetry - Exposure is estimated from biomonitoring data by developing exposure scenarios and running PBPK models in reverse

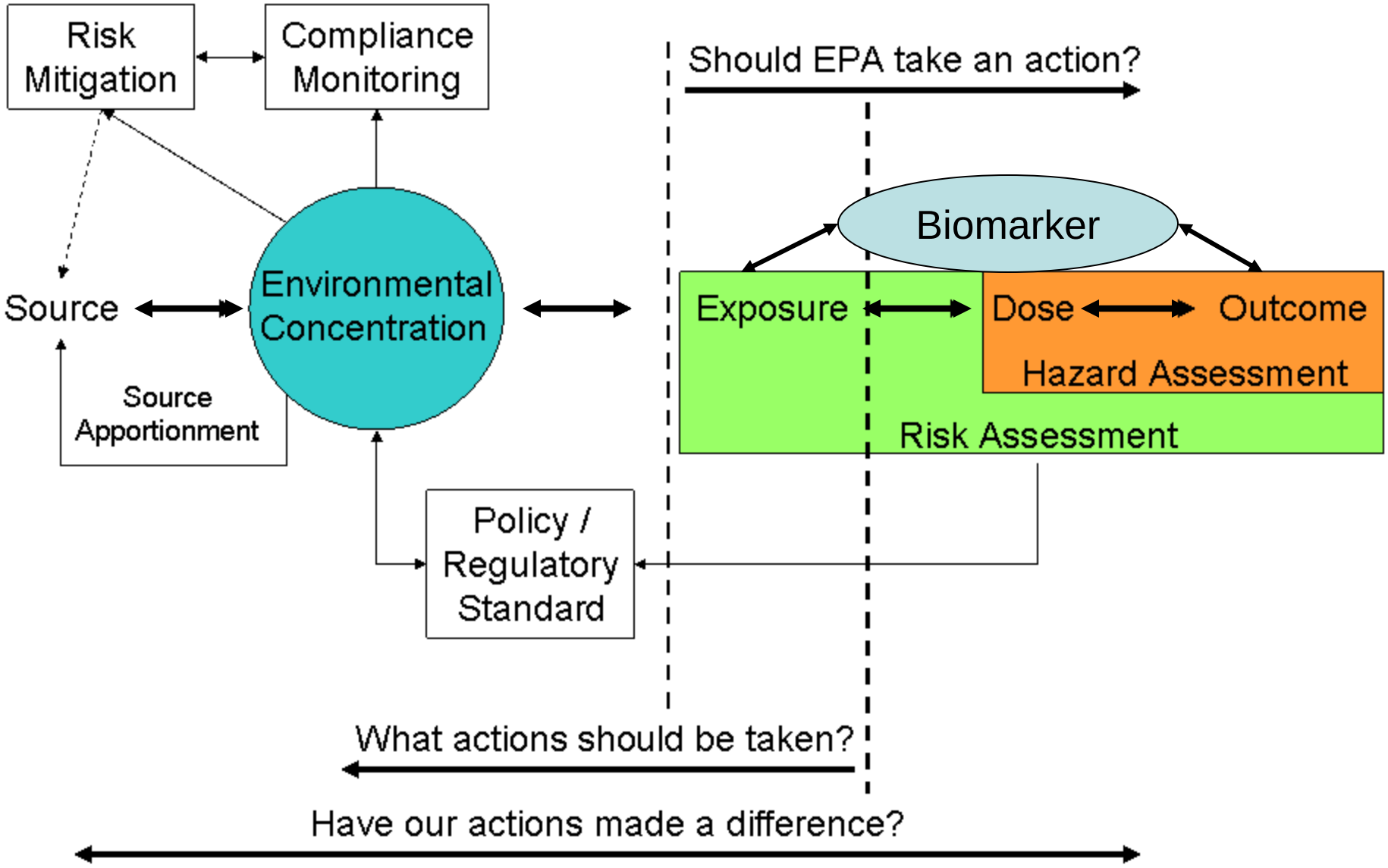
Biomarkers in EPA Decision Making

EPA regulations and standards focus on pollutant sources and environmental concentrations

Effective use of biomonitoring data in risk assessment and risk mitigation requires:

- ***Not only*** **understanding relationships between biomarkers, tissue doses and health outcomes**
- ***But also*** **understanding relationships between biomarker levels, exposures, environmental concentrations and sources (Interpretation)**

Framework for Protecting Public Health and the Environment – Looking Ahead



Drivers for Using Biomonitoring Data

- Readily available, high quality, distributional data
  - NHANES biomonitoring data provides probability distributions of the US population for biomarker concentrations
- Environmental or personal exposure data are not available or feasible
  - i.e., microbials in water

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Biomonitoring in Risk Assessment

Biomonitoring in Risk Assessment

- Traditional Risk Assessments compares
  - Quantitative estimate of human exposure – i.e., estimated daily dose to
  - Acceptable daily dose –Dose (exposure)/response relationship for a toxic endpoint
- How can biomarkers be used for this comparison

Biomarker	⟷	Exposure
Exposure	⟷	Exposure
Biomarker	⟷	Biomarker

The closer the human exposure estimate is to the toxicity endpoint the more accurate the exposure estimate must be

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Approaches for using Biomonitoring in Risk Assessments (NRC,2006)

- **Biomonitoring-based risk assessments**
- **Biomonitoring-led risk assessments**
- **Biomonitoring informs risk assessments**

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Biomonitoring-Based Risk Assessments

- Epidemiology studies that use biomarkers
  - Biomarker/ toxic response directly available
  - Lead and mercury are best examples
  - New opportunities through NCS

Biomonitoring-led Risk Assessment

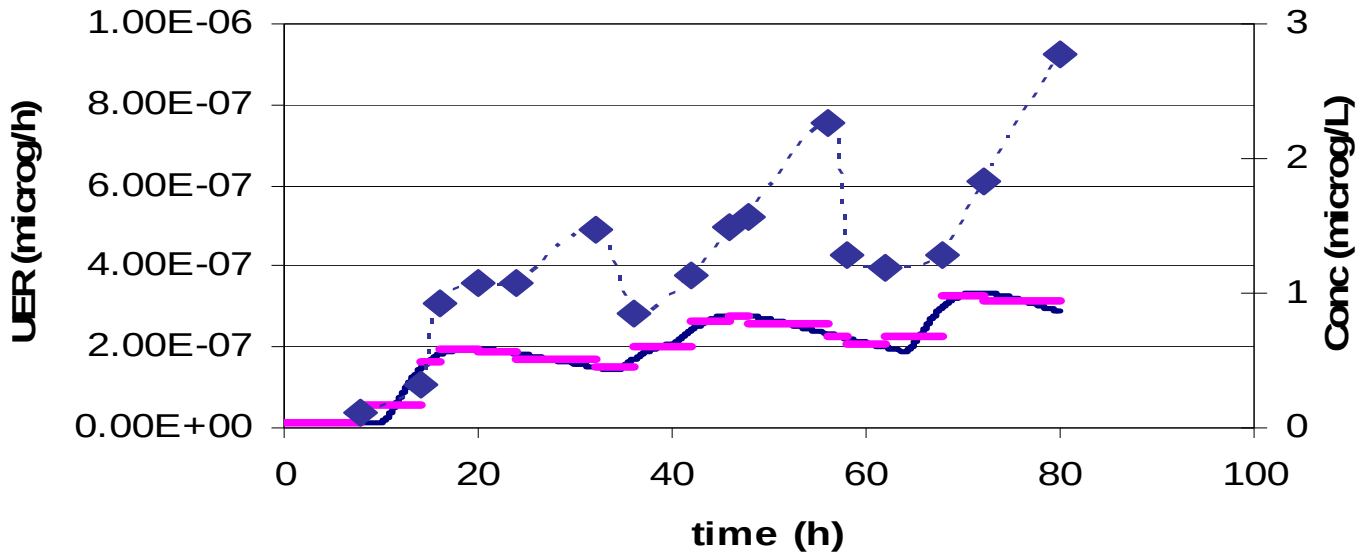
- Conditions:
  - human biomonitoring and animal exposure/response data are robust
  - Few exposure data or epidemiological data
- Approach
  - Convert human biomonitoring data to human exposure estimate using PBPK models
  - Convert animal exposure to animal biomonitoring estimate using PBPK
- Alternative Approach
  - Collect sufficient animal biomonitoring data during toxicity studies

Biomonitoring-led Risk Assessment

- Current Successes-
  - Lipid-soluble, bioaccumulative chemicals
    - Dioxin
    - PFOA
- Areas for improvement
  - Non-lipid soluble, short-half-life chemicals
  - Urine based biomarkers
  - Chemicals with biomarkers as metabolites
  - Chemicals with intermittent exposures
  - Pesticides, (pyrethroids, OPs, carbamates) phthalates, phenols, metals

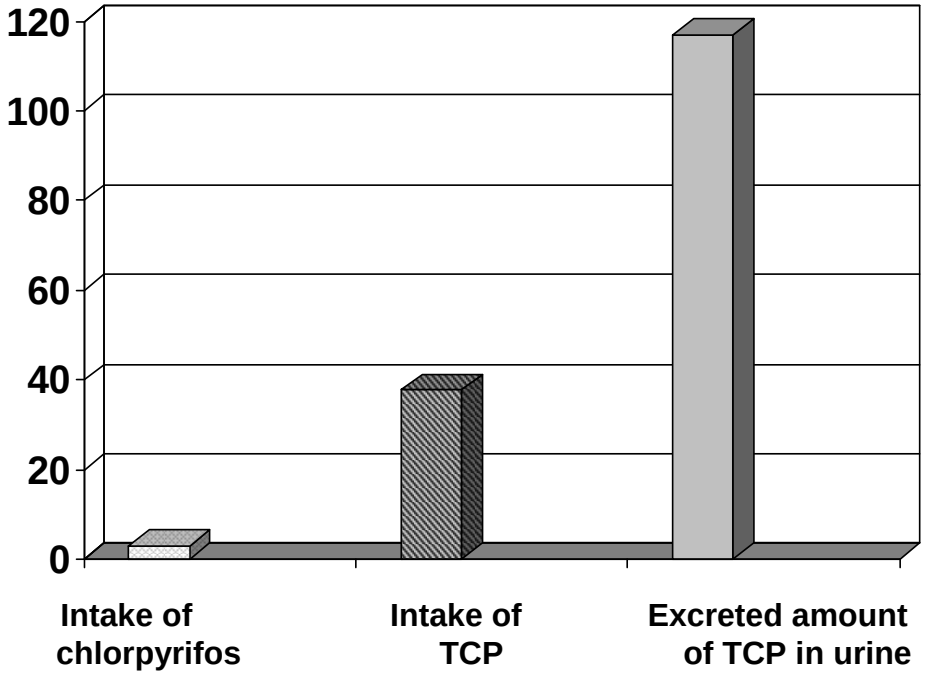
Critical Information

- Good PBPK models with ADME
- Reliable sampling methods - estimate urinary output not just concentrations
- Good information on within person variability – intermittent vs steady state exposure



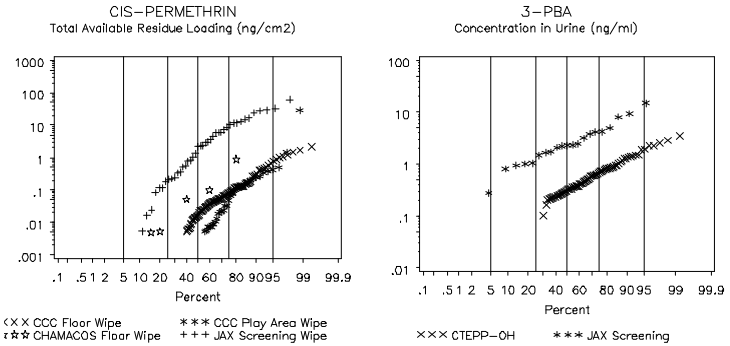
Critical Information

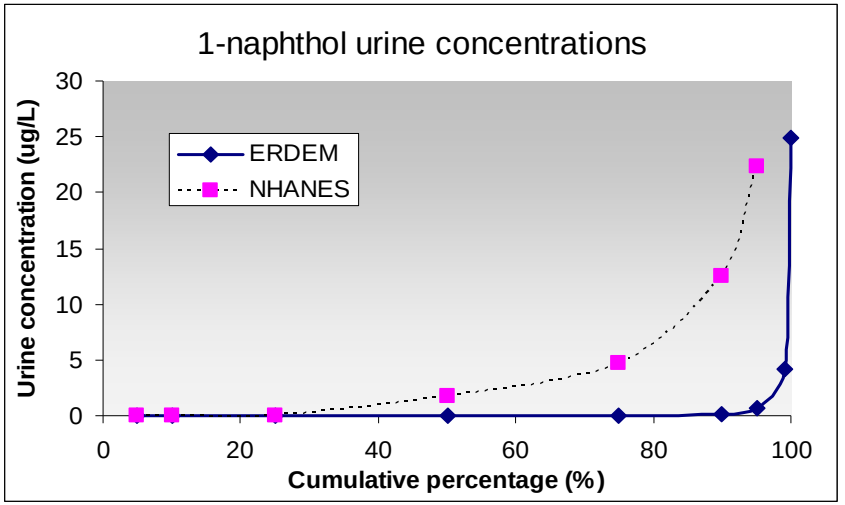
- Biomarkers must be specific for exposure
  - Chlorpyrifos and TCP
  - Arsenic and wood preservative CCA
- High fractional excretion of metabolite-phthalates



Biomonitoring to Inform Risk Assessment

- Screening level assessments
- Demonstrate range and variability of exposures
- ID highly exposed groups and hypothesize conditions for exposure
- Evaluate our assumptions and results
- Identify uncertainties, data gaps, critical research





Biomonitoring to Inform Risk Assessment

- Biomonitoring Equivalents (Hayes et al., 2006)
- Converts health criteria exposures (RfD, MRL, TDI) to a biomarker level
- Uses forward dosimetry to estimate biomarker concentrations from
  - Known external exposures or exposure scenarios
  - Other information – ADME, activity pattern,exposure factors
  - Uses PBPK or mass balance to estimate biomarker
- "Serves as a basis for interpreting biomonitoring results for specific chemical in a health risk context"

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Biomonitoring in Risk Management

Biomonitoring in Risk Management

- Risk management requires information on
  - Exposure and route
  - Source and pathway
- Also requires a metric for regulation
  - Ambient concentration
  - Allowable emission
- This requires linking biomonitoring to exposure then back to a regulatory metric

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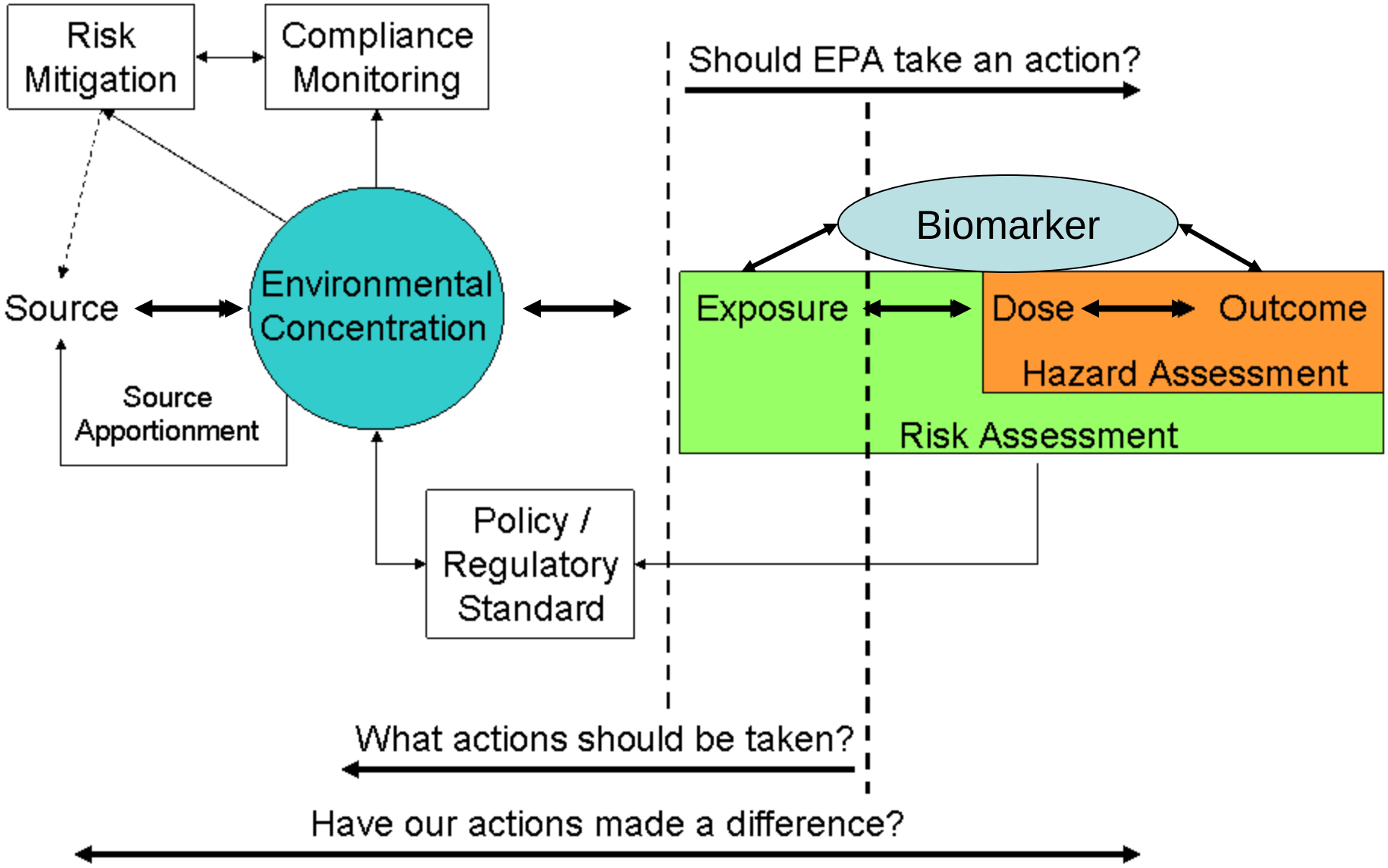

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Reverse Dosimetry Approaches

- Estimate exposure from biomarker using PBPK models in reverse
- Estimate environmental concentrations from exposure using exposure models in reverse
- Tan et al.
  - Analysis of Chloroform
- Kim et al.
  - Analysis of Naphthalene

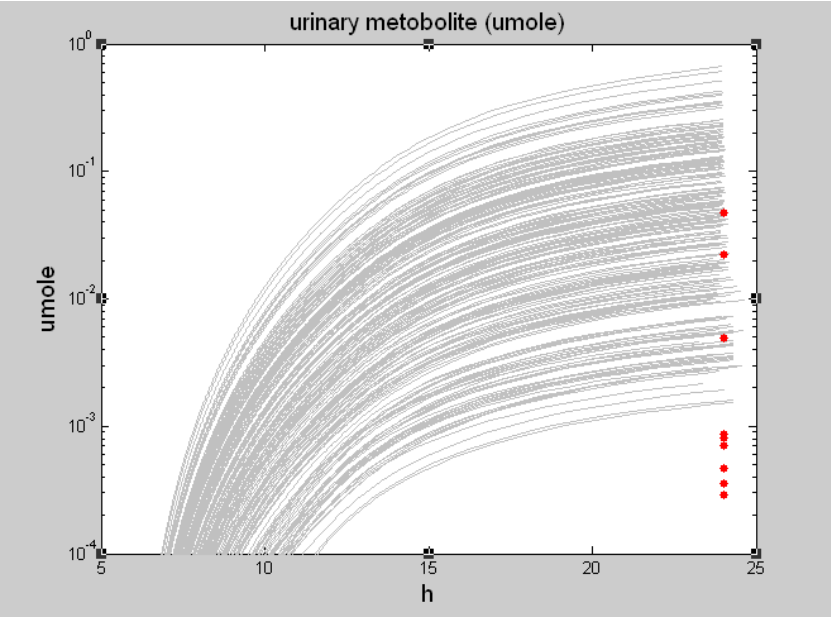
Forward Dosimetry

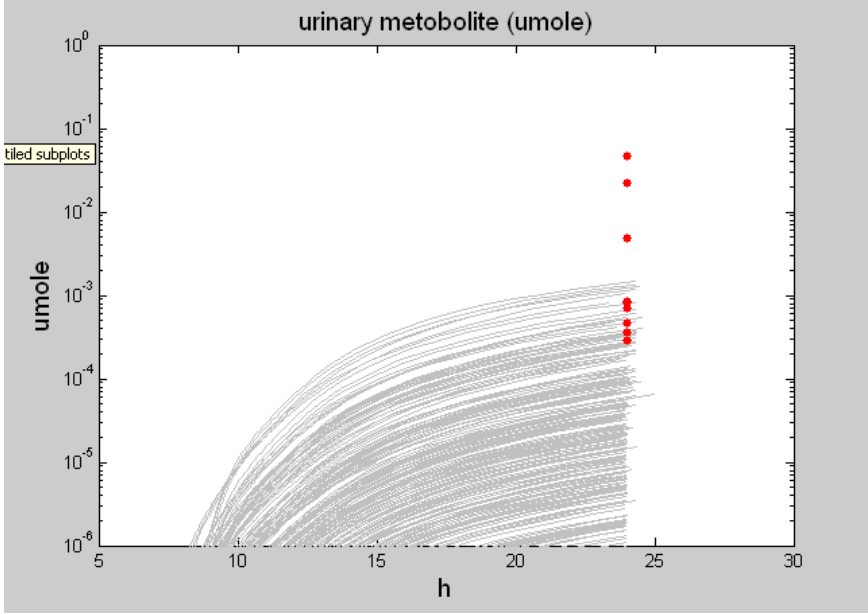
- Biomarkers combined with PBPK models inform pathways
  - Compare biomarkers levels estimated from forward dosimetry to population data
- PBDEs – Lorber et.al,
  - Demonstrated importance of dust ingestion
- Dioxins – Lorber et.al,
  - Demonstrated importance of breast feeding in infants

Biomarkers inform pathways- Permethrins

Hand-to-mouth: Mean of simulation consistent with highest urinary levels

Dermal: minor contribution compared with oral route





200 Monte Carlo simulations varying exposure model parameters

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Biomonitoring in Risk Management

- Potential Use of Source Apportionment with Biomarkers

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Biomonitoring in Accountability

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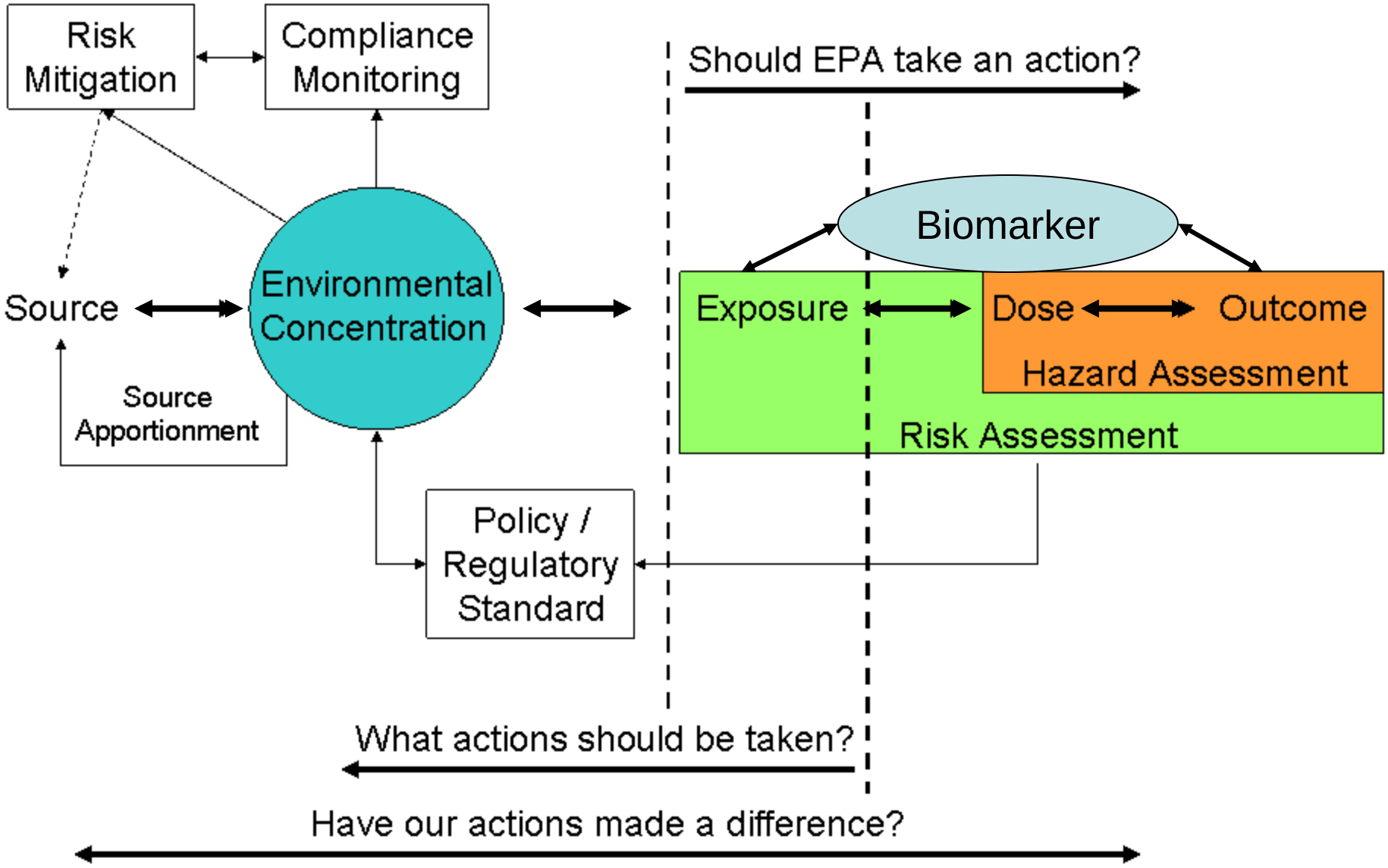

Summary

- Biomonitoring has and *will* play a critical role in environmental decision making
- Full potential requires an integration of the science to answer risk questions, to identify uncertainties, and to develop research programs
  - Questionnaires-extant data
    - Sources and patterns of use
    - Human characteristics and activities
  - Environmental and personal measurement data
  - Exposure models
  - PBPK models
  - Exposure biomarkers